Reprogramming Human Retinal Pigmented Epithelial Cells to Neurons Using Recombinant Proteins.

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Public Summary:
Cells can be reprogrammed to become a different cell type by changing the cell's gene expression. This can be brought about by altering the repertoire of proteins called transcription factors that control gene expression. In this study we use a new method to deliver the transcription factor SOX2 to retinal pigmented epithelial (RPE) cells. We can make RPE cells from stem cells. We demonstrated that RPE cells can be directly reprogrammed to a neuronal fate by introduction of SOX2. The resulting neural cells had the properties expected for a neuron. This might be a way to make different cells that are needed for therapies to treat injury and disease.

Scientific Abstract:
Somatic cells can be reprogrammed to an altered lineage by overexpressing specific transcription factors. To avoid introducing exogenous genetic material into the genome of host cells, cell-penetrating peptides can be used to deliver transcription factors into cells for reprogramming. Position-dependent C-end rule (CendR) cell- and tissue-penetrating peptides provide an alternative to the conventional cell-penetrating peptides, such as polyarginine. In this study, we used a prototypic, already active CendR peptide, RPARPAR, to deliver the transcription factor SOX2 to retinal pigmented epithelial (RPE) cells. We demonstrated that RPE cells can be directly reprogrammed to a neuronal fate by introduction of SOX2. Resulting neuronal cells expressed neuronal marker mRNAs and proteins and downregulated expression of RPE markers. Cells produced extensive neurites and developed synaptic machinery capable of dye uptake after depolarization with potassium. The RPARPAR-mediated delivery of SOX2 alone was sufficient to allow cell lineage reprogramming of both fetal and stem cell-derived RPE cells to become functional neurons.